Mark Chee et al.
Application No.: 08/856,376
Page 8

PATENT

30. The segment of claim 1, wherein the polymorphic site is at a position selected from the group consisting of 15043, 15067, 15110, 15119, 15136, 15217, 15244, 15301, 15431 and 15629.

31. The segment of claim 1, wherein the polymorphic site is at a position selected from the group consisting of 15734, 15784, 15849, 15883, 15902, 16093, 16111, 16114, 16124 and 16126.

32. The segment of claim 1, wherein the polymorphic site is at a position selected from the group consisting of 16129, 16145, 16148, 16264, 16278, 16290, 16318, 16319, and 16354.

33. The segment of claim 1, wherein the polymorphic site is at a position selected from the group consisting of 16362, 16390 and 16519.

## REMARKS

Table 1 has been amended to correct a discrepancy in base numbering between the present application and the reference mitochondrial sequence of Anderson et al. In brief, the mitochrondrial sequence begins in accordance with convention at nucleotide 1. By contrast, the nucleotide sequence in previous table 1 began with the first nucleotide being numbered as zero. Accordingly, in the amended table, each position has been increased by one to conform to the numbering system of Anderson et al. The error was an obvious one when the reference nucleotides shown in Table 1 are compared with nucleotides at the corresponding positions of the Anderson et al. sequence. Moreover, the application specifically discloses that applicants intended to use the same numbering as Anderson et al. (see specification at p. 10, lines 8-13). Therefore, the correction does not constitute new matter. The new dependent claims specify groups of about ten polymorphic positions from those listed in Table 1 (as amended).

### 35 USC 112, second paragraph

Dependency of claims 5-7 has been corrected has been corrected. Dependency of claim 8 is corrected by the correction to claim 7.

Claims 1 and 9 have been amended to recite "perfect" complement as requested by the Examiner. It is submitted that the specification inherently discloses perfect complements of the sequences of Table 1. Mitochondrial DNA is inherently double stranded, and as with other double-stranded sequences, mitochrondrial DNA is conventionally represented by showing only a single strand, it being understood that the other strand is the perfect complement of the strand presented.

### Rejection of claim 4 under 102(b) over Sigma Chemical Catalog

The Examiner says that an oligonucleotide in the Sigma catalog would hybridize notwithstanding a one base mismatch to a segment overlapping position 315. This rejection has been rendered moot by specifying that the allele specific oligonucleotide is perfectly complementary to its target strand (see, p. 11, first paragraph for support).

Attached hereto is a marked-up version of the changes made to the specification by the amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400.

Respectfully submitted,

Joe Liebeschuetz
Reg. No. 37,505

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, 8th Floor
San Francisco, California 94111-3834
Tel: (650) 326-2400
Fax: (650) 326-2422
JOL:pfh
PA 3147029 v1

PATENT

*OIPE*  
*JUN 2 2 2001*  
*PATENT & TRADEMARK OFFICE*
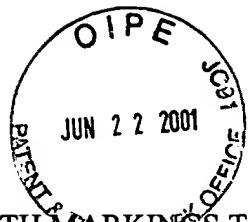
VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The table on pages 30-33 has been amended as follows:

**Table 1**

| pos | rbase | asn base | HA001_ v_mt2 | HA002_ v_mt2 | HA004_ v_mt2 | HA007_ v_mt2 | IB013_ v_mt2 | IGF002_ _v_mt2 | IGF005_ _v_mt2 | IGF007_ _v_mt2 | HA001_ v_mt2 | YR019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 634 | C | c | C | C | T | C | C | C | C | C | C | C |
| 723 | G | a | G | G | A | G | G | G | G | G | G | G |
| 923 | A | a | A | g | G | G | A | A | A | A | A | A |
| 1812 | C | c | T | T | c | T | c | t | C | C | C | C |
| 1945 | T | t | c | C | t | C | t | c | T | C | C | C |
| 2345 | G | a | A | A | g | A | a | A | A | A | A | A |
| 2467 | G | g | G | G | A | G | a | G | G | G | G | G |
| 2967 | A | a | A | A | A | A | G | A | A | A | A | A |
| 3156 | G | g | G | G | G | G | A | G | G | G | G | G |
| 3245 | C | c | C | T | C | T | C | C | C | C | C | C |
| 6623 | G | a | A | A | A | A | A | A | A | A | A | A |
| 67980 | T | t | T | C | T | C | T | T | T | T | T | T |
| 7089 | G | g | A | A | G | A | G | A | G | G | G | G |
| 7689 | G | g | A | a | a | a | a | A | G | A | A | a |
| 8245 | T | t | T | T | A | T | A | T | T | T | T | T |
| 10178 | G | g | A | A | A | A | A | A | G | A | A | A |
| 103940 | T | t | T | T | T | C | T | T | T | T | T | T |
| 10478 | C | c | C | C | T | C | C | C | C | C | C | C |
| 14412 | G | g | A | A | G | A | G | A | G | G | G | G |
| 17056 | C | c | T | C | C | C | C | T | C | C | C | C |
| 17356 | G | a | A | A | A | A | A | A | A | A | A | A |
| 23578 | A | a | G | A | A | A | A | G | A | A | A | A |
| 24156 | T | t | t | t | T | t | T | A | T | n | t | t |
| 27578 | G | g | G | G | A | G | A | G | G | G | G | G |
| 27889 | C | c | C | C | C | C | C | C | C | T | T | T |
| 28845 | T | t | T | T | C | T | C | T | T | T | T | T |
| 300910 | G | g | G | G | G | G | G | G | G | G | G | A |
| 3199200 | T | t | T | A | T | A | T | T | T | T | T | T |
| 33356 | T | t | T | T | T | T | T | T | T | T | C | T |
| 33367 | G | g | G | A | G | G | G | G | G | G | G | G |
| 344950 | C | c | C | C | C | C | C | C | T | C | C | C |
| 35156 | C | c | C | C | A | C | C | C | C | C | C | C |
| 35934 | C | c | T | T | T | t | c | T | C | T | T | T |
| 36478 | C | c | T | C | C | C | C | C | C | C | C | C |
| 36656 | G | g | G | G | G | G | A | G | G | G | G | G |
| 37445 | G | g | G | A | G | G | G | G | G | G | G | G |
| 38656 | T | t | T | T | C | T | T | T | T | T | T | T |
| 39178 | G | g | G | G | G | G | G | G | G | A | A | G |
| 41034 | A | a | G | G | G | G | G | G | A | G | G | G |
| 41578 | A | a | G | A | A | A | A | G | A | A | A | A |
| 42478 | C | t | T | T | T | T | T | T | T | T | T | T |

| pos | rbase | asn_base | HA001_v_mt2 | HA002_v_mt2 | HA004_v_mt2 | HA007_v_mt2 | IB013_v_mt2 | IGF002_v_mt2 | IGF005_v_mt2 | IGF007_v_mt2 | HA001_v_mt2 | YR019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 43112 | C | c | C | C | T | C | C | C | C | C | C | C |
| 45856 | T | t | T | T | C | T | T | T | T | T | T | T |
| 47667 | A | a | G | A | A | A | A | G | A | A | A | A |
| 48234 | G | a | A | A | A | A | A | A | A | A | A | A |
| 49667 | T | t | T | T | T | C | T | T | T | T | T | T |
| 50267 | C | c | T | C | C | C | C | T | C | C | C | C |
| 50956 | T | t | T | T | C | T | T | T | T | T | T | T |
| 51467 | G | g | G | G | G | G | G | G | G | G | A | G |
| 52301 | G | g | G | G | A | G | G | G | G | G | G | G |
| 52512 | G | g | G | G | G | G | G | G | G | G | G | A |
| 52845 | A | a | A | A | A | A | A | A | A | g | G | A |
| 53301 | C | c | A | C | C | C | C | A | C | C | C | C |
| 545960 | G | g | G | G | A | G | G | G | G | G | G | G |
| 56023 | C | c | C | C | T | C | C | C | C | C | C | C |
| 57723 | G | g | G | G | G | G | G | G | A | G | G | G |
| 58134 | T | t | C | T | T | T | T | C | T | T | T | T |
| 58223 | A | a | A | A | A | G | A | A | A | A | A | A |
| 59112 | C | c | T | C | C | C | C | C | C | C | C | C |
| 60701 | T | t | T | T | T | T | C | T | T | T | T | T |
| 614950 | G | g | G | G | G | G | A | G | G | G | G | G |
| 62367 | C | c | C | C | C | C | C | C | T | C | C | C |
| 62523 | T | t | T | T | T | T | C | T | T | T | T | T |
| 65267 | G | a | A | A | A | A | A | A | A | A | A | A |
| 66134 | T | t | C | T | T | T | T | C | T | T | T | T |
| 66623 | A | a | A | A | A | A | A | A | A | A | A | G |
| 67123 | C | c | T | C | C | C | C | T | C | C | C | C |
| 68056 | A | a | G | A | A | A | A | G | A | A | A | A |
| 68267 | T | t | T | C | T | T | T | T | T | T | T | T |
| 68745 | C | c | C | C | C | C | C | C | C | A | C | C |
| 71456 | A | a | A | A | G | A | G | A | A | A | A | A |
| 71745 | T | t | T | T | T | T | T | T | T | C | C | C |
| 72556 | C | c | T | T | T | T | T | T | C | T | T | T |
| 72734 | C | c | C | C | C | C | C | C | C | T | T | T |
| 73889 | T | t | T | T | T | T | C | T | T | T | T | T |
| 75178 | A | a | A | n | A | G | a | a | A | N | A | A |
| 75201 | G | g | A | c | A | G | g | g | G | A | A | A |
| 76234 | T | t | A | A | T | A | T | A | T | T | T | T |
| 77701 | A | a | A | A | A | A | A | A | A | G | G | g |
| 80267 | A | g | G | G | G | G | A | G | G | G | G | G |
| 807980 | C | c | T | C | C | C | C | T | C | C | C | C |
| 82056 | G | g | A | A | G | A | G | A | G | A | A | A |
| 83867 | G | g | A | G | G | G | G | A | G | G | G | G |
| 84278 | C | c | C | C | T | C | C | C | C | C | C | C |
| 84678 | C | c | c | C | T | C | T | C | C | C | c | C |
| 85023 | T | t | C | T | T | c | T | C | T | T | T | T |
| 85656 | A | a | A | A | G | A | A | A | A | A | A | A |
| 86545 | C | c | C | C | T | C | T | C | C | C | C | C |
| 87001 | A | a | G | G | G | G | G | G | G | G | G | G |
| 87834 | A | a | A | A | A | A | G | A | A | A | A | A |
| 87934 | T | c | C | C | C | C | C | C | C | C | C | C |
| 88534 | G | g | G | G | G | G | G | G | G | G | G | A |
| 88767 | T | t | T | T | T | T | C | T | T | T | T | T |

Mark Chee et al.  
Application No.: 08/856,376  
Page 12

PATENT

| pos | rbase | asn_base | HA001_v_mt2 | HA002_v_mt2 | HA004_v_mt2 | HA007_v_mt2 | IB013_v_mt2 | IGF002_v_mt2 | IGF005_v_mt2 | IGF007_v_mt2 | HA001_v_mt2 | YR019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 90412 | C | c | C | C | T | C | C | C | C | C | C | C |
| 90712 | A | a | A | A | A | A | G | A | A | A | A | A |
| 92201 | A | a | G | G | A | G | A | G | A | G | G | G |
| 93467 | A | a | A | A | G | A | A | A | A | A | A | A |
| 94489 | C | c | C | C | C | C | C | C | T | C | C | C |
| 98178 | C | c | C | C | T | C | C | C | C | C | C | C |
| 100301 | T | t | T | T | T | T | C | T | T | T | T | T |
| 101145 | T | t | C | C | T | c | T | C | T | C | C | T |
| 103201 | T | t | T | T | T | T | C | T | T | T | T | T |
| 103723 | G | g | G | G | G | G | G | G | A | G | G | G |
| 105856 | G | g | G | G | g | G | A | G | G | G | G | G |
| 106634 | C | c | C | C | T | C | C | C | C | C | C | C |
| 106878 | G | g | G | G | A | G | A | G | G | G | G | G |
| 107923 | C | c | C | C | C | C | T | C | C | C | C | C |
| 1080910 | T | t | T | T | C | T | C | T | T | T | T | T |
| 108278 | T | t | T | T | T | T | C | T | T | T | T | T |
| 108723 | T | t | C | C | C | C | C | C | C | C | C | C |
| 109145 | T | t | T | T | C | T | T | T | T | T | t | T |
| 111634 | A | a | A | A | A | A | G | A | A | A | A | A |
| 111756 | A | g | G | G | A | G | G | G | G | G | G | G |
| 116401 | A | a | A | A | G | A | A | A | A | A | A | A |
| 116534 | A | a | A | A | A | A | G | A | A | A | A | A |
| 11799800 | A | a | A | A | A | A | A | A | G | A | A | A |
| 119134 | G | g | G | G | A | G | G | G | G | A | A | A |
| 119434 | T | t | C | C | T | C | T | C | T | C | C | C |
| 120067 | A | g | G | G | A | G | G | G | G | G | G | G |
| 120489 | C | c | C | C | C | C | T | C | C | C | C | C |
| 121145 | C | c | C | C | C | C | T | C | C | C | C | C |
| 122356 | G | g | A | A | G | A | G | A | G | G | G | G |
| 123534 | T | t | T | T | T | T | T | T | T | T | T | C |
| 124767 | T | t | T | T | T | T | C | T | T | T | T | T |
| 1271920 | A | a | A | A | G | A | A | A | A | A | A | A |
| 127767 | A | a | G | A | A | A | A | A | A | A | A | A |
| 1280910 | A | a | A | A | A | A | G | A | A | A | A | A |
| 129478 | A | a | G | A | A | A | A | G | A | A | A | A |
| 131045 | A | a | A | A | G | A | G | A | G | A | A | A |
| 131489 | A | a | A | A | A | A | G | A | A | A | A | A |
| 131834 | T | t | T | T | T | C | T | T | T | T | T | T |
| 132023 | A | a | A | A | A | G | A | A | A | A | A | A |
| 132756 | A | a | A | A | G | A | A | A | A | A | A | A |
| 134845 | A | a | A | A | A | A | G | A | A | A | A | A |
| 135056 | C | c | C | C | T | C | t | C | C | C | C | C |
| 1358990 | G | g | a | A | G | A | G | A | G | A | A | A |
| 1364950 | C | c | t | t | t | t | T | T | C | T | T | t |
| 137889 | T | t | T | T | T | T | C | T | T | T | t | T |
| 138023 | A | a | A | A | A | A | A | A | A | g | G | g |
| 139134 | C | c | C | C | C | C | C | C | A | C | C | C |
| 139578 | G | g | G | C | G | C | G | G | G | G | G | G |
| 139656 | A | a | G | A | A | A | A | G | A | A | A | A |
| 139994000 | T | t | T | T | T | T | A | T | T | T | T | T |
| 140589 | A | a | G | A | A | A | A | G | A | A | A | A |
| 141778 | T | t | T | T | T | T | C | T | T | T | T | T |

| pos | rbase | asn _base | HA001_ v_mt2 | HA002_ v_mt2 | HA004_ v_mt2 | HA007_ v_mt2 | IB013_ v_mt2 | IGF002_ v_mt2 | IGF005_ v_mt2 | IGF007_ v_mt2 | HA001_ v_mt2 | YR019 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 143078 | T | t | T | T | C | T | T | T | T | T | T | T |
| 144067 | C | c | T | C | C | C | C | T | C | C | C | C |
| 1455960 | G | g | G | G | G | G | A | G | G | G | G | G |
| 145656 | A | a | A | A | A | A | A | A | A | G | G | G |
| 149101 | C | c | C | C | C | C | T | C | C | C | C | C |
| 150423 | G | g | G | G | G | A | G | G | G | G | G | G |
| 150667 | T | t | T | T | T | T | C | T | T | T | T | T |
| 1510910 | G | g | A | A | G | A | G | A | G | G | G | G |
| 151189 | G | g | G | G | G | G | G | G | G | G | G | A |
| 151356 | C | c | C | C | T | C | C | C | C | C | C | C |
| 152167 | G | g | A | A | G | A | G | A | G | G | G | G |
| 152434 | A | a | A | A | A | A | A | A | A | G | G | A |
| 153001 | G | g | A | A | G | A | G | A | a | A | A | A |
| 154301 | G | g | G | G | A | G | G | G | G | G | G | G |
| 156289 | T | t | T | T | T | T | T | T | T | C | C | T |
| 157334 | G | g | G | G | G | G | G | G | G | G | G | A |
| 157834 | T | t | T | T | T | T | T | T | T | C | C | C |
| 158489 | C | c | C | T | C | T | C | C | C | C | C | C |
| 158823 | G | g | G | G | G | G | G | G | A | G | G | G |
| 159012 | A | a | A | A | A | A | A | A | G | A | A | A |
| 160923 | T | t | T | T | T | T | C | T | T | T | T | T |
| 161101 | T | c | C | C | C | C | C | C | C | C | C | C |
| 161134 | C | c | A | C | C | C | C | A | C | C | C | C |
| 161234 | T | t | t | T | T | T | T | T | C | T | T | T |
| 161256 | T | t | t | T | T | T | T | T | T | T | C | T |
| 161289 | G | g | A | G | A | G | G | G | G | G | G | G |
| 161445 | G | g | G | G | G | G | G | A | G | G | G | G |
| 161478 | C | c | C | C | T | C | C | C | C | C | C | C |
| 162634 | C | c | C | C | C | T | c | C | C | C | c | C |
| 162778 | C | c | T | T | C | T | t | T | T | t | T | T |
| 1628990 | T | c | C | C | C | C | t | C | C | t | c | c |
| 163178 | A | a | A | G | a | A | A | A | A | A | A | A |
| 163189 | A | g | G | G | g | G | G | G | G | G | G | G |
| 163534 | C | c | T | C | C | C | C | T | C | C | C | C |
| 163612 | C | t | T | T | C | T | T | T | C | T | T | T |
| 1638990 | G | g | A | a | G | a | G | A | G | A | A | A |
| 165189 | T | t | T | T | C | T | c | T | C | C | C | C |

## IN THE CLAIMS

1. (Amended)  A segment of human mitochondrial DNA or RNA of between 10 and 100 bases including any one of the polymorphic sites shown in Ftable 1, wherein the polymorphic site within the segment is occupied by a base other than the base shown in Table 1, column 3 ("asn base") or the perfect complement of the segment.

4. (Amended)  An allele-specific oligonucleotide that [hybridizes] is perfectly complementary to a segment of human mitochondrial nucleic acid or its perfect complement

including a polymorphic site shown in Table 1, column 1, wherein the polymorphic site within the

segment is occupied by a base other than the base shown in Table 1, column 3 ("asn" base).

5. (Amended)  The allele-specific oligonucleotide of claim [10] 4 that is a probe.

6. (Amended)  The allele-specific oligonucleotide of claim [10] 4, wherein a central

position of the probes aligns with the polymorphic site of the fragment.

7. (Amended)  The allele-specific oligonucleotide of claim [10] 4 that is a primer.

9. (Amended)  An isolated nucleic acid comprising a segment of at least 10

contiguous bases from SEQ ID NO: 30, or the perfect complement thereof, including a polymorphic

site shown in Table 1, wherein the polymorphic site within the segment is occupied by a base other

than the base shown in Table 1, column 3 ("asn base").